

REPLACEMENT SHEET

1/32

Figure 1

M K H L W F F L L L V A A P R
GAC ATG AAA CAC CTG TGG TTC CTC CTC CTC CTG GTG GCA GCC CCC AGA

W V L S +1 Q V Q L Q E A G P G L V
TGG GTC TTG TCC CAG GTG CAG CTG CAG GAG GCG GGC CCA GGA CTG GTG

K P S E T L S 20 L T C S V S G G S
AAG CCT TCG GAG ACC CTG TCC CTC ACC TGC AGT GTC TCT GGT GGC TCC

I S G D Y Y W F W I R Q S P G K 40
ATC AGC GGT GAC TAT TAT TGG TTC TGG ATC CCC CAG TCC CCA GGG AAG

G L E W I G Y I Y G S G G G T N 60
GGA CTG GAG TGG ATC GGC TAC ATC TAT GGC AGT GGT GGG GGC ACC AAT

Y N P S L N N R V S I S I D T S 70
TAC AAT CCC TCC CTC AAC AAT CGA GTC TCC ATT TCA ATA GAC ACG TCC

K N L F S L K L R S V T A 90
AAG AAC CTC TTC TCC CTG AAA CTG AGG TCT GTG ACC GCC GCG GAC ACG

A V Y Y C A S N I L K Y L H W L 100
GCC GTC TAT TAC TGT GCG AGT AAT ATA TTG AAA TAT CTT CAC TGG TTA

110 L Y W G Q G V L V T V S S 120
TTA TAC TGG GGC CAG GGA GTC CTG GTC ACC GTC TCC TCA (SEQ ID NO:1)

REPLACEMENT SHEET

2/32

Figure 2

M A W A L L L L G L L A H F T
ACC ATG GCC TGG GCT CTG CTG CTC CTC GGC CTC CTT GCT CAC TTT ACA

D S A A +1 S Y E L S Q P R S 10 V S V
GAC TCT GCG GCC TCC TAT GAG TTG AGT CAG CCT CGC TCA GTG TCC GTG

S P G Q T A G F 20 T C G G D N V G
TCC CCA GGA CAG ACG GCC GGG TTC ACC TGT GGG GGA GAC AAC GTT GGA

R K S V Q W Y Q Q K P P 40 Q A P V
AGG AAA AGT GTA CAG TGG TAC CAG CAG AAG CCA CCG CAG GCC CCT GTG

L V I Y A D S E R P S G I P A R 60
CTG GTC ATC TAT GCT GAC AGC GAA CGG CCC TCA GGG ATC CCT CGC CGA

F S G S N S G N T A T L T I S G 70
TTC TCT GGC TCC AAC TCA GGG AAC ACC GCC ACC CTG ACC ATC AGC GGG

V E A G D E A D Y Y C Q V 90 W D S
GTC GAG GCC GGG GAT GAG GCT GAC TAT TAC TGT CAG GTG TGG GAC AGT

T A D H W V F G G G T R L T V L 100
ACT GCT GAT CAT TGG GTC TTC GGC GGA GGG ACC CGG CTG ACC GTC CTA

109
G
GGT (SEQ ID NO:3)

REPLACEMENT SHEET

3/32

Figure 3

Frame 1 Met Ala Trp Ala Leu Leu Leu Leu Gly Leu Leu Ala His Phe Thr Asp Ser Ala Ala
 ATG GCC TGG GCT CTG CTC GGC CTC CTT GCT CAC TTT ACA GAC TCT GCG GCC
 9 18 27 36 45 54

Ser Tyr Glu Leu Ser Gln Pro Arg Ser Val Ser Val Pro Gly Gln Thr Ala Gly Phe Thr
 TCC TAT GAG TTG AGT CAG CCT CGC TCA GNG TCC GTG TCC CCA GGA CAG ACG GCC GGG TTC ACC
 66 75 84 93 102 111 120

Cys Gly Gly Asp Asn Val Gly Arg Lys Ser Val Gln Trp Tyr Gln Gln Lys Pro Pro Gln Ala
 TGT GGG GGA GAC AAC GTT GGA AGG AAA AGT GTC CAG TGG TAC CAG CAG AAG CCA CCG CAG GCC
 129 138 147 156 165 174 183

Pro Val Leu Val Ile Tyr Ala Asp Ser Glu Arg Pro Ser Gly Ile Pro Ala Arg Phe Ser Gly
 CCT GTG CTG GTC ATC TAT GCT GAC AGC GAA CGG CCC TCA GGG ATC CCT GCG CGA TTC TCT GGC
 192 201 210 219 228 237 246

Ser Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Val Glu Ala Gly Asp Glu Ala Asp
 TCC AAC TCA GGG AAC ACC GCC ACC CTG ACC ATC AGC GGG GTC GAG GCC GGG GAT GAG GCT GAC
 255 264 273 282 291 300 309

Tyr Tyr Cys Gln Val Trp Asp Ser Thr Ala Asp His Trp Val Phe Gly Gly Gly Thr Arg Leu
 TAT TAC TGT CAG GTG TGG GAC AGT ACT GCT GAT CAT TGG GTC TTC GGC GGA GGG ACC CGG CTG
 318 327 336 345 354 363 372

Thr Val Leu Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
 ACC GTC CTA GGT CAG CCC AAG GCT GCC CCC TCG GTC ACT CTG TTC CCG CCC TCC TCT GAG GAG
 381 390 399 408 417 426 435

Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr
 CTT CAA GCC AAC TAC GTG TGT CTC ATA AGT GAC TTC TAC CGG GGA GCC GTG ACA
 444 453 462 471 480 489 498

Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys
 GTG GCC TGG AAG GCA GAT AGC AGC CCC GTC AAG CGG GGA GTG GAG ACC ACC ACA CCC TCC AAA
 507 516 525 534 543 552 561

Gln Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser
 CAA AGC AAC AAC TAC GCG GCC AGC AGC TAC AGC TCG AGC CCT GAG CAG TGG AAG TCC
 570 579 588 597 606 615 624

His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr Val Ala Pro
 CAC AGA AGC TAC AGC TGC CAG GTC AGC CAT GAA GGG AGC ACC GTG GAG AAG ACA GTG GCC CCT
 633 642 651 660 669 678 687

Thr Glu Cys Ser TTR
 ACA GAA TGT TCA TGA (SEQ ID NO:5)

REPLACEMENT SHEET

4/32

Figure 4

Frame 1 Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp Val Leu Ser
 ATG AAA CAC CTG TGG TTC CTC CTC CTG GTG GCA GCC CCC AGA TGG GTC TTG TCC
 9 18 27 36 45 54

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr
 CAG GTG CAG CTG CAG GAG TCG GGC CCA GGA CTG GTG AAG CCT TCG GAG ACC CTG TCC CTC ACC
 66 75 84 93 102 111 120

Cys Ser Val Ser Gly Gly Ser Ile Ser Gly Asp Tyr Tyr Trp Phe Trp Ile Arg Gln Ser Pro
 TGC AGT GTC TCT GGT GGC TCC ATC AGC GGT GAC TAT TAT TGG TTC TGG ATC CGC CAG TCC CCA
 129 138 147 156 165 174 183

Gly Lys Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Gly Ser Gly Gly Gly Thr Asn Tyr Asn Pro
 GGG AAG GGA CTG GAG TGG ATC GGC TAC ATC TAT GGC AGT GGT GGG GGC ACC AAT TAC AAT CCC
 192 201 210 219 228 237 246

Ser Leu Asn Asn Arg Val Ser Ile Ser Ile Asp Thr Ser Lys Asn Leu Phe Ser Leu Lys Leu
 TCC CTC AAC AT CGA GTC TCC ATT TCA ATA GAC ACG TCC AAG AAC CTC TTC TCC CTG AAA CTG
 255 264 273 282 291 300 309

Arg Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Ser Asn Ile Leu Lys Tyr Leu
 AGG TCT GTG ACC GCC GCG GAC ACG GCC GTC TAT TAC TGT GCG AGT AAT ATA TTG AAA TAT CTT
 318 327 336 345 354 363 372

His Trp Leu Leu Tyr Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 CAC TGG TTA TTA TAC TGG GGC CAG GGA GTC GTC ACC GTC TCC TCA GCT AGC ACC AAG GGC
 381 390 399 408 417 426 435

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly
 CCA TCC GTC TTC CCC CTG GCG CCC TGC TCC AGG AGC ACC TCC GAG AGC ACA GCC GGC CTG GGC
 444 453 462 471 480 489 498

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
 TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG AGC TCG TGG AAC TCA GGC GCC CTG ACC
 507 516 525 534 543 552 561

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
 AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA CTC TAC TCC CTC AGC AGC GTG
 570 579 588 597 606 615 624

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro
 GTG ACC GTG CCC TCC AGC AGC ATG GGC ACG AAC ACC TAC ACC TGC AAC GTA GAT CAC AAG CCC
 633 642 651 660 669 678 687

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro

REPLACEMENT SHEET

5/32

Figure 4 (Continued)

AGC AAC ACC AAG GTG	GAC AAG AGA GTT	GAG TCC AAA TAT	GGT CCC CCA TGC	CCA TCA TCA TGC	CCA	
696	705	714	723	732	741	750

Ala Pro Glu Phe Leu	Gly Gly Pro Ser Val	Phe Leu Phe Pro Pro	Lys Pro Lys Asp Thr	Leu		
GCA CCT GAG TTC CTG	GGG GGA CCA TCA	GTC TTC CCC CCA AAA	CCC AAG GAC ACT	CTC		
759	768	777	786	795	804	813

Met Ile Ser Arg Thr	Pro Glu Val Thr Cys	Val Val Val Asp Val	Ser Gln Glu Asp Pro	Glu		
ATG ATC TCC CGG ACC	CCT GAG GTC ACG TGC	GTC GTG GTG GAC GTG	AGC CAG GAA GAC CCC GAG			
822	831	840	849	858	867	876

Val Gln Phe Asn Trp	Tyr Val Asp Gly Val	Glu Val His Asn Ala	Lys Thr Lys Pro Arg	Glu		
GTC CAG TTC AAC TGG	TAC GTG GAT GGC	GTG GAG GTG CAT AT	GCC AAG ACA AAG CCG CGG GAG			
885	894	903	912	921	930	939

Glu Gln Phe Asn Ser	Thr Tyr Arg Val Val	Ser Val Leu Thr Val	Leu His Gln Asp Trp	Leu		
GAG CAG TTC AAC AGC	ACG TAC CGT GTG GTC	AGC GTC CTC ACC GTC	CTG CAC CAG GAC TGG CTG			
948	957	966	975	984	993	1002

Asn Gly Lys Glu Tyr	Lys Cys Lys Val Ser	Asn Lys Gly Leu Pro	Ser Ser Ile Glu Lys Thr			
AAC GGC AAG GAG TAC	AAG TGC AAC AAA GGC	CTC CCG TCC TCC	ATC GAG AAA ACC			
1011	1020	1029	1038	1047	1056	1065

Ile Ser Lys Ala Lys	Gly Gln Pro Arg Glu	Pro Gln Val Tyr Thr	Leu Pro Pro Ser Gln	Glu		
ATC TCC AAA GCC AAA	GGG CAG CCC CGA	GGG CCA CGG GTG	TAC ACC CTG CCC CCA TCC CAG GAG			
1074	1083	1092	1101	1110	1119	1128

Glu Met Thr Lys Asn Gln	Val Ser Leu Thr Cys	Leu Val Lys Gly Phe	Tyr Pro Ser Asp Ile			
GAG ATG AAC AAC CAG	GTC AGC CTG ACC TGC	GTC AAA GGC TTC	TAC CCC AGC GAC ATC			
1137	1146	1155	1164	1173	1182	1191

Ala Val Glu Trp Glu	Ser Asn Gly Gln Pro	Glut Asn Asn Tyr Lys	Thr Thr Pro Pro Val	Leu		
GCC GTC GAG TGG	Glut AAC GAT GGG	CAG COG GAG AAC	TAC AAG ACC ACG CCT	CCC GTG CTG		
1200	1209	1218	1227	1236	1245	1254

Asp Ser Asp Gly Ser	Phe Leu Tyr Ser Arg	Leu Thr Val Asp	Lys Ser Arg Trp	Gln Glu		
GAC TCC GAC GGC	TCC TTC CTC TAC	AGC AGG CTA ACC	GTG GAC AAG AGC	TGG CAG GAG		
1263	1272	1281	1290	1299	1308	1317

Gly Asn Val Phe Ser	Cys Ser Val Met His	Glu Ala Leu His Asn	His Tyr Thr Gln	Lys Ser		
GGG AAT GTC TTC	TCA TGC TCC ATG	CAT GAG GCT	CTG CAC AAC CAC	TAC ACA CAG AAG AGC		
1326	1335	1344	1353	1362	1371	1380

Leu Ser Leu Ser Leu	Gly Lys TER			
CTC TCC CTG TCT	CTG GGT AAA TGA	(SEQ ID NO:7)		
1389	1398			

REPLACEMENT SHEET

6/32

Figure 5

Frame 1 Met Lys His Leu Trp Phe Phe Leu Leu Val Ala Ala Pro Arg Trp Val Leu Ser
 ATG AAA CAC CTG TGG TTC CTC CTC CTG GTG GCA GCC CCC AGA TGG GTC TTG TCC
 9 18 27 36 45 54

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr
 CAG GTG CAG CTG CAG GAG TCG GGC CCA GGA CTG GTG AAG CCT TCG GAG ACC CTG TCC CTC ACC
 66 75 84 93 102 111 120

Cys Ser Val Ser Gly Gly Ser Ile Ser Gly Asp Tyr Tyr Trp Phe Trp Ile Arg Gln Ser Pro
 TGC AGT GTC TCT GGT GGC TCC ATC AGC GGT GAC TAT TAT TGG TTC TGG ATC CGC CAG TCC CCA
 129 138 147 156 165 174 183

Gly Lys Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Gly Ser Gly Gly Gly Thr Asn Tyr Asn Pro
 GGG AAG GGA CTG GAG TGG ATC GGC TAC ATC TAT GGC AGT GGT GGG GGC ACC AAT TAC AAT CCC
 192 201 210 219 228 237 246

Ser Leu Asn Asn Arg Val Ser Ile Ser Ile Asp Thr Ser Lys Asn Leu Phe Ser Leu Lys Leu
 TCC CTC AAC AAT CGA GTC TCC ATT TCA ATA GAC ACG TCC ARG AAC CTC TTC TCC CTG AAA CTG
 255 264 273 282 291 300 309

Arg Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Ser Asn Ile Leu Lys Tyr Leu
 AGG TCT GGG ACC GCC GCG GAC ACG GCC GTC TAT TAC TGT GCG AGT AAT ATA TTG AAA TAT CTT
 318 327 336 345 354 363 372

His Trp Leu Leu Tyr Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 CAC TGG TTA TTA TAC TGG GGC CAG GGA GTC CTG GTC ACC GTC TCC TCA GCT AGC ACC AAG GGG
 381 390 399 408 417 426 435

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly
 CCA TCC GTC TTC CCC CTG GCG CCC TGC TCC AGG AGC ACC TCC GAG AGC ACA GGC CCC CTG GGC
 444 453 462 471 480 489 498

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
 TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG TGG AAC TCA GGC GCC CTG ACC
 507 516 525 534 543 552 561

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
 AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA CTC TAC TCC CTC AGC AGC GTG
 570 579 588 597 606 615 624

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro
 GTG ACC GTG CCC TCC AGC AGC TTG GGC ACG AAC ACC TAC ACC TGC AAC GTC GAT CAC AAG CCC
 633 642 651 660 669 678 687

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro

REPLACEMENT SHEET

7/32

Figure 5 (Continued)

AGC AAC ACC AAG GTG GAC AAG AGA GTT GAG TCC AAA TAT GGT CCC CCA TGC CCA TCA TCA TGC CCA	696	705	714	723	732	741	750
---	-----	-----	-----	-----	-----	-----	-----

Ala Pro Glu Phe Glu Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu	GCA CCT GAG TTC GAG GGG GGA CCA TCA GTC TTC CTG TCC CCC CCA AAA CCC AAG GAC ACT CTC	759	768	777	786	795	804	813
---	---	-----	-----	-----	-----	-----	-----	-----

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu	ATG ATC TCC CGG ACC CCT GAG GTC ACG TGC GTG GTG GAC GTG AGC CAG GAA GAC CCC GAG	822	831	840	849	858	867	876
---	---	-----	-----	-----	-----	-----	-----	-----

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu	GTC CAG TTC AAC TGG TAC GTG GAT GGC GTG GAG GTG CAT AAT GCC AAG ACA AAG CCG CGG GAG	885	894	903	912	921	930	939
---	---	-----	-----	-----	-----	-----	-----	-----

Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu	GAG CAG TTC AAC AGC ACG TAC CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG	948	957	966	975	984	993	1002
---	---	-----	-----	-----	-----	-----	-----	------

Asn Gln Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr	AAC GGC AAG GAG TAC AAG TGC AAC AAA GGC CTC CCG TCC TCC ATC GAG AAA ACC	1011	1020	1029	1038	1047	1056	1065
---	---	------	------	------	------	------	------	------

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu	ATC TCC AAA GCC AAA GGG CAG CCC CGA GAG CCA CAG GTG TAC ACC CTG CCC CCA TCC CAG GAG	1074	1083	1092	1101	1110	1119	1128
---	---	------	------	------	------	------	------	------

Glu Met Thr Lys Asn Gln Val Ser Leu Val Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile	GAG ATG ACC AAC CAG GTC AGC TCG ACC TGC AAC TAC AAA GGC TTC TAC CCC AGC GAC ATC	1137	1146	1155	1164	1173	1182	1191
---	---	------	------	------	------	------	------	------

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu	GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAC ACC ACG CCT CCC GTG CTG	1200	1209	1218	1227	1236	1245	1254
---	---	------	------	------	------	------	------	------

Asp Ser Asp Gly Ser Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu	GAC TCC GAC GGC TCC TTC CTC TAC AGC AGG CTA ACC GTG GAC AAG AGC AGG TGG CAG GAG	1263	1272	1281	1290	1299	1308	1317
---	---	------	------	------	------	------	------	------

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser	GGG AAT GTC TTC TCA TGC TCC GTG ATG CAT GAG GCT CTG CAC AAC CAC TAC ACA CAG AAG AGC	1326	1335	1344	1353	1362	1371	1380
---	---	------	------	------	------	------	------	------

Leu Ser Leu Ser Leu Gly Lys TER	(SEQ ID NO:9)
CTC TCC CTG TCT CTG GGT AAA TGA	1389
	1398

REPLACEMENT SHEET

8/32

Figure 6

Frame 1 Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp Val Leu Ser
ATG AAA CAC CTG TGG TTC CTC CTC CTG GTG GCA GCC CCC AGA TGG GTC TTG TCC
9 18 27 36 45 54

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr
CAG GTG CAG CTG CAG GAG TCG GGC CCA GGA CTG GTG AAG CCT TCG GAG ACC CTG TCC CTC ACC
66 75 84 93 102 111 120

Cys Ser Val Ser Gly Gly Ser Ile Ser Gly Asp Tyr Tyr Trp Phe Trp Ile Arg Gln Ser Pro
TGC AGT GTC TCT GGT GGC TCC ATC AGC GGT GAC TAT TAT TGG TTC TGG ATC CGC CAG TCC CCA
129 138 147 156 165 174 183

Gly Lys Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Gly Ser Gly Gly Gly Thr Asn Tyr Asn Pro
GGG AAC GGA CTG GAG TGG ATC GGC TAC ATC TAT GGC AGT GGT GGG GGC ACC AAT TAC AAT CCC
192 201 210 219 228 237 246

Ser Leu Asn Asn Arg Val Ser Ile Ser Ile Asp Thr Ser Lys Asn Leu Phe Ser Leu Lys Leu
TCC CTC AAC AAT CGA GTC TCC ATT TCA ATA GAC ACG TCC AAG AAC CTC TTC TCC CTG AAA CTG
255 264 273 282 291 300 309

Arg Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Ser Asn Ile Leu Lys Tyr Leu
AGG TCT GTG ACC GCC GCG GAC ACG GCC GTC TAT TAC TGT GCG AGT AAT ATA TTG AAA TAT CTT
318 327 336 345 354 363 372

His Trp Leu Leu Tyr Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
CAC TGG TTA TTA TAC TGG GGC CAG GGA GTC GTC ACC GTC TCC TCA GCT AGC ACC AAC AAG GGG
381 390 399 408 417 426 435

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly
CCA TCC GTC TCC CCC CTG GCG CCC TGC TCC AGG AGC ACC TCC GAG AGC ACA GGC GCC CTG GGC
444 453 462 471 480 489 498

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
TGC CTG GTC AAG GAC TAC TTC CCC CCG GAA CCG GTG ACG GTG TCG TGG AAC TCA GGC GCC CTG ACC
507 516 525 534 543 552 561

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA CTC TAC TCC CTC AGC AGC GTG
570 579 588 597 606 615 624

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro
GTG ACC GTG CCC TCC AGC AGC TTG GGC ACG AAG ACC TAC ACC TGC AAC GTA GAT CAC AAG CCC
633 642 651 660 669 678 687

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro

REPLACEMENT SHEET

9/32

Figure 6 (Continued)

AGC AAC ACC AAG GTG GAC AAG AGA GTT GAG TCC AAA TAT GGT CCC CCA TGC CCA CCA TGC CCA	596	705	714	723	732	741	750
---	-----	-----	-----	-----	-----	-----	-----

Ala Pro Glu Phe Glu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu	GCA CCT GAG TTC GAG GGG GGA CCA TCA GTC TTC CTG TTC CCC CCA AAA CCC AAG GAC ACT CTC	759	768	777	786	795	804	813
---	---	-----	-----	-----	-----	-----	-----	-----

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu	ATG ATC TCC CGG ACC CCT GAG TGC ACG TGC GTG GTG GAC GTG AGC CAG GAA GAC CCC GAG	822	831	840	849	858	867	876
---	---	-----	-----	-----	-----	-----	-----	-----

Val Glu Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu	GTC CAG TTC AAC TGG TAC GTG GAT GGC GTG GAG GTG CAT AAT GCC AAG ACA AAG CCG CGG GAG	885	894	903	912	921	930	939
---	---	-----	-----	-----	-----	-----	-----	-----

Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu	GAG CAG TTC AAC AGC ACG TAC CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG	948	957	966	975	984	993	1002
---	---	-----	-----	-----	-----	-----	-----	------

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr	AAC GGC AAG GAG TAC AAG TGC AAG GTC TCC AAC AAA GGC CTC CGT TCC TCC ATC GAG AAA ACC	1011	1020	1029	1038	1047	1056	1065
---	---	------	------	------	------	------	------	------

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu	ATC TCC AAA GCC AAA GGG CAG CCC CGA GAG CCA CAG GTG TAC ACC CTG CCC CCA TCC CAG GAG	1074	1083	1092	1101	1110	1119	1128
---	---	------	------	------	------	------	------	------

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile	GAG ATG AAC AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAC CCC AGC GAC ATC	1137	1146	1155	1164	1173	1182	1191
---	---	------	------	------	------	------	------	------

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu	GCC GTG GAG TGG GAG AGC AAT GGG CAG CGG GAG AAC AAC TAC AAG ACC AGC CCT CCC GTG CTG	1200	1209	1218	1227	1236	1245	1254
---	---	------	------	------	------	------	------	------

Asp Ser Asp Gly Ser Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu	GAC TCC GAC GGC TCC TTC CTC TAC AGC AGG CTA ACC GTG GAC AAG AGC AGG TGG CAG GAG	1263	1272	1281	1290	1299	1308	1317
---	---	------	------	------	------	------	------	------

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser	GGG AAT GTC TTC TCA TGC TCC GTG ATG CAT GAG GCT CTG CAC AAC CAC TAC ACA CAG AAG AGC	1326	1335	1344	1353	1362	1371	1380
---	---	------	------	------	------	------	------	------

Leu Ser Leu Ser Leu Gly Lys TER	(SEQ ID NO:11)	
CTC TCC CTG TCT CTG GGT AAA TGA	1389	1398

Figure 7-1

5' 'Sense' Primers
Primers for the Amplification of Monkey Immunoglobulin Heavy Chain Variable Regions

A. Human or Monkey heavy chain early leader sequence primers with *Sail* / site

V _H 1	5' ACTAAGTCGACATGGACTGGACCTTGG 3'	(SEQ ID NO:13)
V _H 2	5' ACTAAGTCGACATGGACATACTTGTTCAC 3'	(SEQ ID NO:14)
V _H 3	5' ACTAAGTCGACATGGACATGGAGTTGGGTGAGC 3'	(SEQ ID NO:15)
V _H 4	5' ACTAAGTCGACATGGACATGGAAACACCTGTGGTCTT 3'	(SEQ ID NO:16)
V _H 5	5' ACTAAGTCGACATGGACATGGGTCAACGCCATCT 3'	(SEQ ID NO:17)
V _H 6	5' ACTAAGTCGACATGGTCTCTCCCTCAT 3'	(SEQ ID NO:18)

B. Human or Monkey heavy chain late leader sequence primers with *Mlu* / site

V _H 1	5' g gca gca gc (cm) <u>ACG</u> <u>CGT</u> <u>GCC</u> <u>CAC</u> <u>TCC</u> <u>GAG</u> <u>GT</u> 3' +1	(SEQ ID NO:19)
V _H 2	5' g acc gtc ccc <u>ACG</u> <u>CGT</u> <u>GT</u> (TC) <u>TTG</u> <u>TCC</u> <u>CAG</u> <u>GT</u> 3' +1	(SEQ ID NO:20)
V _H 3	5' gct att ttc <u>ACG</u> <u>CGT</u> <u>GTC</u> <u>CAG</u> <u>TGT</u> <u>GAG</u> 3' +1	(SEQ ID NO:21)
V _H 4	5' gcg gct ccc <u>ACG</u> <u>CGT</u> <u>GTC</u> <u>CTG</u> <u>TCC</u> <u>CAG</u> 3' +1	(SEQ ID NO:22)
V _H 5	5' g gct gtt ctc <u>ACG</u> <u>CGT</u> <u>GTC</u> <u>TGT</u> <u>GAG</u> <u>GT</u> 3' +1	(SEQ ID NO:23)

Figure 7-1 (Continued)

C. Human or Monkey framework 1 sequence primers with *Xho* 1 site

V _H 1,3a,5	+1	CAGGTGCAG <u>CTGCTCGAAGTC</u> CTGG	(SEQ ID NO:24)
V _H 2	+1	CA <u>GGTCAACTTA</u> CTCAGTCAGTCTGG	(SEQ ID NO:25)
V _H 3b	+1	GA <u>GGTGCAGCTGCTCGAAGTC</u> CTGG	(SEQ ID NO:26)
V _H 4	+1	CA <u>GGTGCAGCTGCTCGAAGTC</u> GGG	(SEQ ID NO:27)
V _H 6	+1	CA <u>GGTACAGCTGCTCGAAGTC</u> CGGG	(SEQ ID NO:28)

3'Anti-Sense' PrimersA. Human or Monkey heavy chain constant region primers anti-sense strand with *Nhe* 1 site

IgG ₁₋₄	5'	GGC GGA TGC <u>GCT AGC</u> TGA GGA GAC GG 3'	+110
			Nhe 1
			(SEQ ID NO:29)

Figure 7-2

Primers for the Amplification of Monkey Immunoglobulin Light Chain Variable Regions5' 'Sense' PrimersA. Human or Monkey kappa light chain early leader primers with *Bgl II* site

1. 5' ATCACAGATCTCTCACATGCTGTCAGAGCCAGGTC 3' (SEQ ID NO:30)
2. 5' ATCACAGATCTCTCACATGG(GA)G(AT)CCCC(TA)GC(TG)CAGCT 3' (SEQ ID NO:31)
3. 5' ATCACAGATCTCTCACATGGACATGAGGGTCCCCGCTCAG 3' (SEQ ID NO:32)
4. 5' ATCACAGATCTCTCACATGGACAC(GAC)AGGGCCCCACTCAG 3' (SEQ ID NO:33)

B. Human or Monkey lambda light chain early leader primers with *Bgl II* site

1. 5' ATCACAGATCTCTCACCATGGCCATGGCTCTCTGCTCC 3' (SEQ ID NO:34)
2. 5' ATCACAGATCTCTCACCATGGCTCCACTACTCTC 3' (SEQ ID NO:35)
3. 5' ATCACAGATCTCTCACCATGACCTGCTCCCTCTCTCCTCC 3' (SEQ ID NO:36)
4. 5' ATCACAGATCTCTCACCATGGCTGGAGCTCTCTCTCTC 3' (SEQ ID NO:37)
5. 5' ATCACAGATCTCTCACCATGACTGGACCCCCACTCTC 3' (SEQ ID NO:38)

Figure 7-2 (Continued)

3' 'Anti-Sense' Primers

A. Human or Monkey kappa light chain constant region primer anti-sense strand with *Kpn* 1 and *BsiW1* sites

C_{Kappa} 5' CCG TTT GAT TTC CAG CTT GGT ACC TCC ACC GAA CGT 3',
 (SEQ ID NO:39)
 +108
 Kpn 1

5' TGC AGC ATC CGT ACG TTT GAT TTC CAG CTT 3',
 (SEQ ID NO:40)
 +112
 BsiW1
 +103

B. Human or Monkey lambda light chain constant region primer anti-sense strand with
Kpn 1, *Hind* III and *Avr* II sites

C_{Lambda} 5' ACC TAG GAC GGT AAG CTT GGT ACC TCC GCC 3',
 (SEQ ID NO:41)
 +107
 Hind III
 Kpn 1

5' ACC TAG GAC GGT CA (C/G) (C/G) TT GGT ACC TCC GCA CAC 3',
 (SEQ ID NO:42)
 +107
 Kpn 1

5' CTT GGG CTG ACC TAG GAC GGT GAG CCG 3',
 (SEQ ID NO:43)
 +110
 Avr II
 +102

Figure 8

A. Heavy chain variable region:

B. Heavy chain constant region anti-sense strand:

IgM	5'	T	⁺¹¹⁹ TGG	GGC	GGA	TGC	⁺¹¹⁵ ACT	3'
IgG _{1,4}	5'	GA	⁺¹¹⁹ TGG	GCC	CTT	GGT	⁺¹¹⁵ GGA	3'

C. Light chain variable region:

Kappa	5' G ATG ACC CAG TCT CCA (G/T) CC TC 3'	+4	+10	(SEQ ID NO:52)
Lambda	5' CTC A (C/T)T(T/C) (G/A) C TGC (A/C) CA GGG TCC 3'	-9	-3	(SEQ ID NO:53)

D. Light chain constant region anti-sense strands:

5' AA GAC AGA TGG TGC AGC CA 3'	+115	+110	(SEQ ID NO:54)
5' G GAA CAG AGT GAC CGA GGG G 3'	+118	+112	(SEQ ID NO:55)

Figure 16

PCR Primers for Human $\gamma 4$ Constant Region

1) IDEC 462 3' PCR Primer
5' GGGG GGA TCC TCA TTT ACC CAG AGA CAG GG 3'
BamHI (SEQ ID NO:56)

2) IDEC 479 5' PCR Primer
5' GGGG GCT AGC ACC AAG GGC CCA TCC GTC TTC 3'
Nhe I (SEQ ID NO:57)

PCR Mutagenesis of Human $\gamma 4$

3) IDEC 698 3' PCR Primer
5' CCG GGA GAT CAT GAG AGT GTC CTT GGG TTT TGG GGG GAA CAG GAA GAC
BspHI Glu Pro (SEQ ID NO:58)

TGA TGG CCC CTC GAA CTC AGG TGC TGG GCA TGG TGG GCA TGG GGG 3'

4) Midland GE212 5' PCR Primer
5' TCC TCA GCT AGC ACC AAG GGG CCA TCC 3'
Nhe I Destroys Apa I site (SEQ ID NO:59)

REPLACEMENT SHEET

23/32

Figure 17

Frame 1 Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp Val Leu Ser
ATG AAA CAC CTG TGG TTC TTC CTC CTC CTG GTG GCA GCC CCC AGA TGG GTC TTG TCC
9 18 27 36 45 54

+1
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr
CAG GTG CAG CTG CAG GAG TCG GGC CCA GGA CTG GTG AAG CCT TCG GAG ACC CTG TCC CTC ACC
66 75 84 93 102 111 120

Cys Ser Val Ser Gly Gly Ser Ile Ser Gly Asp Tyr Tyr Trp Phe Trp Ile Arg Gln Ser Pro
TGC AGT GTC TCT GGT GGC TCC ATC AGC GGT GAC TAT TAT TGG TCC ATC CGC CAG TCC CCA CCA
129 138 147 156 165 174 183

Gly Lys Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Gly Ser Gly Gly Gly Thr Asn Tyr Asn Pro
GGG AAG GGA CTG GAG TGG ATC GGC TAC ATC TAT GGC AGT GGT GGG GGC ACC AAT TAC AAT CCC
192 201 210 219 228 237 246

Ser Leu Asn Asn Arg Val Ser Ile Ser Ile Asp Thr Ser Lys Asn Leu Phe Ser Leu Lys Leu
TCC CTC AAC AAT CGA GTC TCC ATT TCA ATA GAC ACG TCC AAC AAC CTC TTC TCC CTG AAA CTG
255 264 273 282 291 300 309

Arg Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Ser Asn Ile Leu Lys Tyr Leu
AGG TCT GTG ACC GCC GCG GAC ACG GCC GTC TAT TAC TGT GCG AGT AAT ATA TTG AAA TAT CTT
318 327 336 345 354 363 372

His Trp Leu Leu Tyr Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
CAC TGG TTA TTA TAC TGG GGC CAG GGA GTC CTG GTC ACC GTC TCC TCA GCT AGC ACC AAC AAG GGG
381 390 399 408 417 426 435

Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly
CCA TCC GTC TCC CCC CTG GCG CCC TGC TCC AGG AGC ACC TCC GAG AGC ACA GCC GGC CTG GGC
444 453 462 471 480 489 498

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
TGC CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG AAC TCA GGC GCC CTG ACC
507 516 525 534 543 552 561

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
AGC GGC GTG CAC ACC TTC CGG GCT GTC CTA CAG TCC TCA GGA CTC TAC TCC AGC AGC GTG
570 579 588 597 606 615 624

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro
GTG ACC GTG CCC TCC AGC AGC TTG GGC ACG AGC ACC TAC ACC TGC AAC GTA GAT CAC AAG CCC
633 642 651 660 669 678 687

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro

REPLACEMENT SHEET

24/32

Figure 17 (Continued)

AGC AAC ACC AAG GTG GAC AAG AGA GTT GAG TCC AAA TAT GGT CCC CCA TGC CCA CCA TGC CCA	696	705	714	723	732	741	750
---	-----	-----	-----	-----	-----	-----	-----

Ala Pro Glu Phe Glu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu	GCA CCT GAG TTC GAG GGG GGA CCA TCA GTC TTC CTG TTC CCC CCA AAA CCC AAG GAC ACT CTC	759	768	777	786	795	804	813
---	---	-----	-----	-----	-----	-----	-----	-----

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu	ATG ATC TCC CGG ACC CCT GAG GTC ACG TGC GTG GTG GAC GTG AGC CAG GAA GAC CCC GAG	822	831	840	849	858	867	876
---	---	-----	-----	-----	-----	-----	-----	-----

Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu	GTC CAG TTC AAC TGG TAC GTG GAT GGC GTG GAG GTG CAT AAT GCC AAG ACA AAG CCG CGG GAG	885	894	903	912	921	930	939
---	---	-----	-----	-----	-----	-----	-----	-----

Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu	GAG CAG TTC AAC AGC ACG TAC CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG	948	957	966	975	984	993	1002
---	---	-----	-----	-----	-----	-----	-----	------

Asn Gln Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Glu Leu Pro Ser Ser Ile Glu Lys Thr	AAC GGC AAC GAG TAC AAC GAG TGC AAC GTC TCC AAC AAA GGC CTC CGG TCC TCC ATC GAG AAA ACC	1011	1020	1029	1038	1047	1056	1065
---	---	------	------	------	------	------	------	------

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu	ATC TCC AAA GCC AAA GGG CAG CCC CGA GAG CCA CAG GTG TAC ACC CTG CCC CCA TCC CAG GAG	1074	1083	1092	1101	1110	1119	1128
---	---	------	------	------	------	------	------	------

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Glu Phe Tyr Pro Ser Asp Ile	GAG ATG ACC AAC AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAC CCC AGC GAC ATC	1137	1146	1155	1164	1173	1182	1191
---	---	------	------	------	------	------	------	------

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu	GCC GTG GAG TGG GAG AAC ATT GGG CAG CGG GAG AAC AAC TAC AAC AGC ACC CCT CCC GTG CTG	1200	1209	1218	1227	1236	1245	1254
---	---	------	------	------	------	------	------	------

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu	GAC TCC GAC GGC TCC TTC CTC TAC AGC AGG CTA ACC GTG GAC AAG AGC AGG TGG CAG GAG	1263	1272	1281	1290	1299	1308	1317
---	---	------	------	------	------	------	------	------

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser	GGG AAT GTC TTC TCA TGC TCC GTG ATG CAT GAG GCT CTG CAC AAC CAC TAC ACA CAG AAG AGC	1326	1335	1344	1353	1362	1371	1380
---	---	------	------	------	------	------	------	------

Leu Ser Leu Ser Leu Gly Lys TER	CTC TCC CTG TCT CTG GGT AAA TGA	1389	1398	(SEQ ID NO:11)			
---------------------------------	---------------------------------	------	------	----------------	--	--	--